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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/164,764    10/01/98    SIDRANSKY    D    01107.76459

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HM12/0824

EXAMINER

SOUAYA, J

ART UNIT

PAPER NUMBER

1655

DATE MAILED: 08/24/01

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

# Office Action Summary

Application No.

09/164,764

Applicant(s)

Sidransky

Examiner

Jehanne Souaya

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on May 15, 2001
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 23-37 is/are pending in the application.
- 4a) Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 24-28, 34, and 37 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some\* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892) 18) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 19) ☐ Notice of Informal Patent Application (PTO-152)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_ 20) ☐ Other:

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### **DETAILED ACTION**

1. Currently, claims 23-37 are pending in the instant application. All the amendments and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance. Any rejections not reiterated are hereby withdrawn. The following rejections are either newly applied or are reiterated. They constitute the complete set being presently applied to the instant Application.

#### ***Maintained Rejections***

##### ***Double Patenting***

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

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Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. Claims 24-28 and 37 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 6,235,470. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are drawn to a method of detecting cancer of any organ in a specimen of body fluid which drains the organ by detecting an alteration in microsatellite marker length alteration. The claims of the '470 patent are drawn to a method of detecting head and neck or lung cancer in a saliva sample from a patient (specimen that contains fluid that drains an organ) by detecting a genetic mutation which can include nucleotide deletion or substitution, or LOH and wherein the target nucleic acid can be a microsatellite marker. Thus these claims read on a microsatellite length alteration (amplification, deletion or LOH at the marker).

***Claim Rejections - 35 USC § 103***

4. Claims 24-28 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brugieres et al (Cancer Research, Feb. 1993, vol. 53, pp 452-455) in view of Gonzalez-Zulueta (Cancer Research 1993) Merlo et al., (Cancer Research 1994), and Ah-See et al (Cancer Research, 1994).

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The claims are drawn to a method of detecting cancer of any organ in a specimen of body fluid which drains the organ by detecting an alteration in microsatellite marker length alteration. Brugieres teaches detecting sarcoma in patients by detecting p53 mutations from DNA isolated from total blood. Although Brugieres does not teach detecting cancer by detecting microsatellite length alterations, it was known in the art at the time of the invention that microsatellite length alterations were associated with different forms of cancer. Gonzalez-Zulueta teaches that instabilities include both tri and tetra-nucleotide repeats and both expansion and deletions of repeat units with the microsatellite markers (p. 5620, lines 2-8). Gonzalez-Zulueta teaches detecting such instabilities in patients with bladder and colorectal cancers and suggests that "this kind of instability might be common to all sporadic human cancers (p. 5622, col. 2, lines 22-29). Merlo et al teaches that microsatellite instability (deletions or expansions) were found to be common in small cell lung cancer (p. 2099). Ah-See teaches that LOH was detected in microsatellite markers in patients with Squamous Carcinoma of the Head and Neck (see abstract). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to detect cancer by detecting microsatellite marker length alterations in a specimen that contains body fluid that drains from an organ. Brugieres teaches detecting sarcoma by detecting DNA mutations from total blood, thus the ordinary artisan would have a reasonable expectation of success that cancer cells could be found in blood and that total blood could be used as a specimen in detecting mutations. From the teachings of Gonzales-Zulueta, Merlo, and Ah-See, the ordinary artisan would have been taught that different types of cancer could be detected

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by detecting microsatellite length alterations and that such instabilities were common in different types of cancer. The ordinary artisan would have been motivated to combine these teachings to arrive at the instantly claimed invention for the purposes of developing a non-invasive (teaching of Brugieres), reliable (teachings that microsatellite length alterations are a reliable indicator of cancer) method of detecting cancer in a patient.

5. Claims 34 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hayashi et al (Cancer Research, July 1994, vol. 54, pp 3853-3856) in view of Gonzalez-Zulueta (Cancer Research 1993) Merlo et al., (Cancer Research 1994), and Ah-See et al (Cancer Research, 1994).

Claim 34 is drawn generally to detecting cancer cells in a specimen external to a primary tumor by detecting microsatellite length alterations in a histopathological margin specimen external to a primary tumor.

Hayashi et al teach that discrepancies were found between genetic and histopathological diagnoses in 7 out of 14 cases with respect to presence or absence of cancer cells in lymph nodes, as these patients were histologically diagnosed node negative by genetically diagnosed node positive (see abstract). Hayashi further teaches detecting mutations in 5 of seven total regional lymph nodes where histopathological diagnosis detected no metastasis (see p. 3854, col 2). Therefore, from the teachings of Hayashi, the ordinary artisan would have been taught that cancer cells can be found in regions external to primary tumors and that such cancer cells are not necessarily detectable by traditional histopathological methods. The ordinary artisan would have

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further been taught the importance of detecting cancer cells in such specimens as Hayashi teaches disease recurs in 20-30% of patients and that therefore, genetic evaluation of lymph nodes for metastasis may become a useful prognosticator.

Although Hayashi does not teach detecting microsatellite length alterations, Gonzalez-Zulueta teaches that instabilities include both tri and tetra-nucleotide repeats and both expansion and deletions of repeat units with the microsatellite markers (p. 5620, lines 2-8). Gonzalez-Zulueta teaches detecting such instabilities in patients with bladder and colorectal cancers and suggests that “this kind of instability might be common to all sporadic human cancers (p. 5622, col. 2, lines 22-29). Merlo et al teaches that microsatellite instability (deletions or expansions) were found to be common in small cell lung cancer (p. 2099). Ah-See teaches that LOH was detected in microsatellite markers in patients with Squamous Carcinoma of the Head and Neck (see abstract). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to detect cancer by detecting microsatellite marker length alterations in a histopathological specimen. Hayashi teaches detecting lymph node metastasis in regional lymph nodes that were histopathologically negative, thus the ordinary artisan would have a reasonable expectation of success that cancer cells could be found in histopathological sections external to a primary tumor and that such could be detected through genetic changes. From the teachings of Gonzales-Zulueta, Merlo, and Ah-See, the ordinary artisan would have been taught that different types of cancer could be detected by detecting microsatellite length alterations and that such instabilities were common in different types of cancer. The ordinary artisan would have


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been motivated to combine these teachings to arrive at the instantly claimed invention for the purposes of developing a reliable (teachings that microsatellite length alterations are a reliable indicator of cancer) and improved method of detecting metastasis in tissue that would traditionally be diagnosed as negative (teaching of Hayashi):

6. Claims 23, 29-32, and 35-36 are free of the prior art.
7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703)308-6565. The examiner can normally be reached Monday-Thursday from 7:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

  
LISA B. ARTHUR  
PRIMARY EXAMINER  
GROUP 1800 1600

  
Jehanne Souaya  
Patent examiner  
July 27, 2001